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Perforator-based interposition flaps
perform better than full thickness skin grafts
for the release of burn scar contractures:
a multicenter randomized controlled trial

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Abstract

Background: Burn scar contractures remain a significant problem for the severely burned patient. Reconstructive surgery is often indicated to improve function and the quality of life. Skin grafts (preferably full thickness grafts) are frequently used to cover the defect that remains after scar release. Local flaps are also used for this purpose and provide, besides healthy skin, subcutaneous tissue. The vascularization and versatility of local flaps can be further improved by enclosing a perforator at the base of the flap. Until now, no randomized controlled trial (RCT) has been performed to determine which technique has the best effectiveness in burn scar contracture releasing procedures.

Materials and Methods: A multicenter RCT was performed to compare the effectiveness of perforator-based interposition flaps to full thickness skin grafts (FTSGs) for the treatment of burn scar contractures. The primary outcome parameter was change in the surface area of the flap or FTSG. Secondary outcome parameters were width, elasticity, color, POSAS, and range of motion. Measurements were performed after 3 and 12 months.

Results: The mean surface area between flaps (N=16) and FTSGs (N=14) differed statistically significant at 3 months (123% vs. 87%, $p<0.001$) and 12 months (142% vs. 92%, $p<0.001$). In terms of the secondary outcome parameters (specifically the POSAS observer score and color), interposition flaps showed superior results to FTSGs.

Conclusions: Perforator-based interposition flaps result in a more effective scar contracture release than FTSGs and should therefore be preferred over FTSGs when possible.

Introduction

Burn scar contractures remain a significant problem in severely burned patients¹. Patients suffering from these contractures often experience considerable limitations in daily life. Therefore surgical treatment is often necessary². Many treatment regimens are available for burn scar contracture release. A recently performed systematic review, however, showed that it is still unclear which technique is the most effective treatment³. In clinical practice, wide scar contractures are regularly treated with a skin graft, which is preferably full thickness (full thickness skin graft, FTSG)⁴. However, their effectiveness in terms of re-contraction has never been objectified in burn patients. The available studies on the contraction rate in other patient groups show that FTSGs have the tendency to re-contract, which could result in partial or total recurrence of the initial problem in burn patients^{5,6}.

Ideally, tissue that does not contract and will grow with the patient is used for the release of scar contractures. For this purpose, locally available tissue is preferred because it provides tissue of superior quality and contains healthy adjacent skin and subcutaneous fat. The safety and versatility of local flaps can be improved by incorporating a perforator bundle. This means that the vascular supply (an artery with concomitant veins) is secured, which is illustrated in *Figure 1*. The discovery that perforators are dispersed throughout the body⁷⁻¹⁰, has led to the development of many perforator-based flaps in specific regions of the body^{11,12}. For example, the thoracodorsal artery flap in the breast-axilla region^{13,14}, and the cervical artery flap in the neck region^{15,16}.

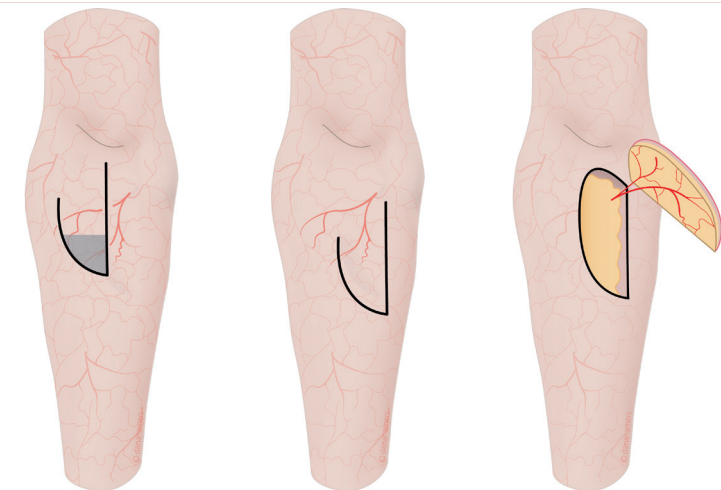


Figure 1. Illustrates the concept of incorporating a perforator in a local flap. In the left image a local flap is designed disregarding the location of the perforator. The grey area represents subsequent necrosis. In the middle, the perforator is localized and the flap is designed in such a way that it incorporates the perforator bundle. The flap may be non-islanded (middle) or islanded (right).

Burn scar contractures occur almost on all body sites, also on locations at where well-known perforators are not available for reconstructive purposes. The so-called ad hoc perforator-based flap may provide a solution here¹⁷. These flaps are based on any perforator adjacent to the contracture that is capable of sufficient blood supply. In a cohort study that was published by our group in 2011, an algorithm was presented describing the use of perforator-based interposition flaps for the treatment of large scar contractures¹⁸. Follow-up measurements of the surface area of these flaps were performed and showed an expansion of 116% after a mean follow-up period of 7.8 months¹⁸. Moreover, two other studies showed that no revision surgery is required with the use of this type of flaps for the reconstruction of scar contractures^{17,19}. Hence, the use of perforator-based interposition flaps for the treatment of scar contractures points towards favorable results. The implications by means of a randomized controlled trial (RCT) however, have yet to be determined. For this reason we performed an RCT in which the effectiveness of perforator-based interposition flaps was compared to FTSGs for the release of scar contractures.

Materials and Methods

Study design and randomization

An open randomized controlled trial was conducted to evaluate the effectiveness of perforator-based interposition flaps compared to FTSGs for scar contracture release. Recruitment took place in two burn centers in the Netherlands (the Red Cross Hospital in Beverwijk and the Martini Hospital in Groningen). All patients gave written informed consent. The study protocol was approved by the national medical ethics committee (M010-070) and registered at clinical trials (no. NCT01409759). This study could not be blinded because the treatment allocation was clearly recognizable by both the patient and the observer.

Patients were randomly assigned to receive either treatment with a perforator-based interposition flap, which will be referred to as flap from now on, or a FTSG. Block randomization, stratified per center, was applied with a randomization ratio of one-to-one to ensure balance of the numbers in each treatment group. To prevent anticipation on the randomization sequence, block sizes of 6 and 4 were used. The order of the blocks was determined with a random numbers table²⁰. To ensure allocation concealment, sequentially numbered opaque sealed envelopes were used. To avoid differences in preoperative work up (including wound bed preparation), the randomization took place during the operation procedure (before releasing the contracture).

Patients

We enrolled patients of 18 years and older with an indication for release of a wide scar contracture. Only patients that had sufficient tissue for a flap were eligible. In addition, patients had to be able to give informed consent. Scars on the face and scalp were excluded.

Surgical procedures

In both groups, the location of suitable perforators was assessed preoperatively using Doppler (Huntleigh Dopplex D900, Cardiff, UK) or Duplex (iU22 Duplex with a L17-5 transducer, Philips, Eindhoven, The Netherlands). Using this approach, we assured that both groups received a uniform preoperative work up, thereby limiting expectancy bias. Presence of scar tissue in the flap or graft was documented.

Once a flap was allocated, we applied the algorithm that was previously published by Verhaegen *et al*¹⁸. In this algorithm, the flap is preferably pedicled resulting in a non-islanded flap, meaning that the skin base is left intact. If the vascularization of the flap appeared to be compromised in the intended position, the flap was converted to an islanded flap. This was primarily a clinical decision that allowed for greater angles of rotation where necessary. The predesigned flap was incised and consisted of cutis and subcutis, hereby preserving the dermal vascular plexus. The flap was mobilized and the viability of the flap was assured in the intended position. If the flap remained viable, it was sutured using subcutaneous and intracutaneous absorbable polyglactin sutures respectively (Vicryl™ 2-0 and Vicryl™ 4-0, Ethicon Johnson and Johnson, USA). The donor site was closed primarily. *Figure 2* and *Figure 3* show two examples of flaps (non-islanded and islanded, respectively).



Figure 2. Example of a 23-year-old patient with a contracture of the head-neck region. A non-islanded perforator flap was performed (left). The photograph on the right represents the flap at a follow-up period of 3 months.



Figure 3. Example of an islanded perforator flap in the neck region of a 56-year-old patient. The photograph on the left shows the flap at 1 week postoperative, the photograph on the right at 3 months postoperative.

In case a FTSG was allocated, the incisions were made following the design. The donor site was chosen at the same location as where the flap would have been sited. Subsequently, the skin - together with a thin layer of subcutaneous fat - was harvested. Defatting of the subcutaneous tissue was performed to facilitate survival of the graft. The graft was fixated using resorbable sutures (Vicryl Rapide™ 3-0, Ethicon Johnson and Johnson, USA) and a tie-over was applied that was removed after seven days.

Primary outcome parameter

The primary outcome parameter was the surface area of the flap or graft after a follow-up period of 3 months and 12 months. This is the most genuine and accurate parameter because it is the least influenced by external factors (such as joint stiffness). To measure the surface area, planimetry was performed by tracing the boundaries of the flap or graft on a transparent, pliable sheet that was subsequently digitized. Planimetric measurements were performed digitally (NIS-elements AR 2.6, Nikon, Amstelveen, the Netherlands). This is a reliable and valid measurement method²¹.

Secondary outcome parameters

Necrosis

Necrosis was defined as a disorder in wound healing resulting in an unhealed wound after 3 weeks. The surface area of necrosis was measured according to the digital tracing method described above.

Width of the flaps

The width of the flaps was measured on a transparent sheet as described previously¹⁸. In short, the width of the non-islanded flaps was measured by drawing a line between both arms of the flap: from the end of the short arm, perpendicular on the long arm. The width of the islanded flaps was assessed by measuring the distance between the long arms at the center of rotation¹⁸. The width of the FTSGs was measured in the center of the graft.

Elasticity and Color

Elasticity measurements were performed using the Cutometer® (Courage & Khazaka GmbH, Cologne, Germany), which is a reliable and valid instrument for the evaluation of skin elasticity²². The Cutometer® provides several elasticity parameters, of which the parameter *elasticity (Ue)* was used. This single parameter was shown to sufficiently represent the elasticity of the tissue²². Color measurements were performed by the DermaSpectrometer, a validated assessment tool for skin erythema (Cortex Technology, Hadsund, Denmark)¹⁴. The results of the DermaSpectrometer represent the extent of color deviation from normal skin. Three to five measurements of the flap or graft were taken, depending on the size of the flap or graft, according to a predefined measurement protocol (Figure 4). The mean of these measurements was used for further analysis.

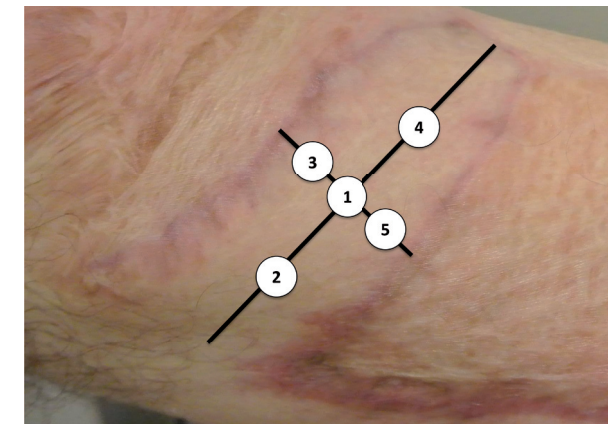


Figure 4. Example of a flap on the left upper arm. According to the standardized measurement protocol, the measured surface area is divided by drawing a line through the horizontal and vertical axis of the surface area. Point 1 was measured at the intersection of these lines. Points 2, 3, 4 and 5 were measured halfway from the intersection to the borders of the surface area.

POSAS

Subjective scar assessment was performed by means of the POSAS²³, a reliable and valid scar assessment tool that consists of two parts; the patient and the observer scale, that numerically scores 6 items on a 10-point rating scale, in which a score of 10 reflects the worst imaginable scar²⁴. A mean score of the observer and the patient was calculated by averaging the 6 separate item scores.

Range of motion

Range of motion was measured in degrees using goniometry according to a standard measurement protocol³. In case motion was limited in more directions, the mean of the measured range of motions was used for further analysis.

Measurement points

Preoperatively, we performed scar elasticity, scar color, POSAS and range of motion measurements, to retrieve baseline data of the contractures. The surface area, width, and percentage of scar tissue included in the flap or graft were measured immediately after surgery. Postoperative complications were also registered. After 3 weeks, an experienced plastic surgeon evaluated the presence of necrosis and performed surface area measurements. After 3 and 12 months, an independent researcher assessed the following outcome parameters: surface area, width, elasticity, color, POSAS and range of motion.

Power analysis and statistics

We performed an *a priori* power analysis (G*Power 3 version 3.0.3.) to estimate the required sample size. For the power analysis, the results of Stephenson *et al.* and Verhaegen *et al.* were used^{5,18}. Stephenson *et al.* documented a decrease in mean surface area of full thickness grafts to 62%⁵. Verhaegen *et al.* demonstrated an increased surface area of 116% for perforator-based interposition flaps¹⁸. In the current study, we considered a remaining surface area of 100% (no contraction) as a clinically significant outcome for the interposition flaps. Therefore, 100% was selected in the power-analysis. The power was set at 0.80 and alpha at 0.05. A sample size of 13 patients per group was calculated. However, in anticipation of a dropout rate, a sample size of 15 patients per group was chosen.

Statistical analysis was performed using SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). Normal distribution was tested by calculating the skewness and kurtosis, evaluating frequency histograms, and performing the Shapiro-Wilk test. This was done for each parameter at each measurement point. Significant differences between independent data were tested using the independent t-test (in case of a normal distribution) or the Mann-Whitney U (MWU) test (in case of a non-normal distribution). To compare categories (POSAS outcomes) for independent data, the Chi-Square test was used. For paired data, the paired t-test was used (normal distribution) or the Wilcoxon signed ranks test (non-normal distribution). The two-tailed significance criterion was set at 0.05.

Results

Baseline characteristics

Patients were recruited from July 2011 until January 2014. *Figure 5* represents a flow diagram that shows the progress through the phases of the trial. Baseline characteristics are presented in *Table 1*. No statistically significant differences were found between the two groups. All patients suffered from post burn scar contractures. One patient had a history of diabetes mellitus. In 9 out of 16 flaps and 3 out of 13 FTSGs, supple scar tissue was included with a mean surface of 29% and 20%, respectively ($p=0.141$, MWU test). No correlation between the inclusion of scar tissue and the incidence of necrosis ($p=0.351$, MWU test) or area of necrosis ($p=0.681$, MWU test) could be demonstrated. In 14 out of 16 flaps the base was left intact.

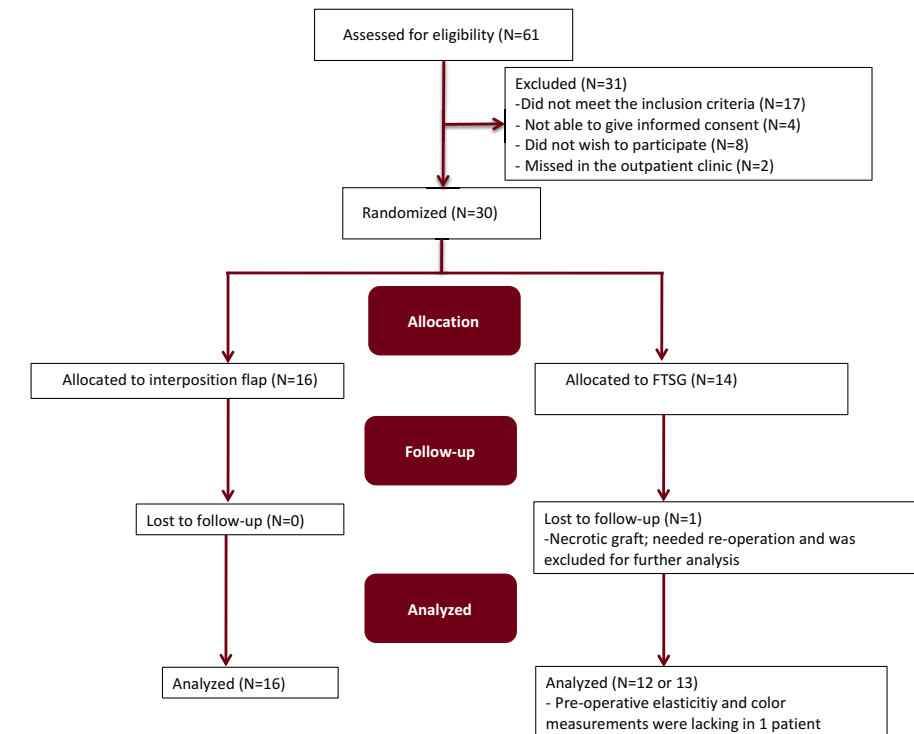


Figure 5. Flow chart of the numbers of patients that were included and measured throughout the course of the study.

Differences between flaps and FTSGs

Figure 6 shows the primary outcome parameters and corresponding p-values. After a mean follow-up period of 3.1 months (SD: 0.7 months), the surface area of the perforator-based interposition flaps increased to 123%, whereas the surface area of the FTSGs decreased to 87% (95% confidence interval of the difference -53 to -19, $p<0.001$, independent t-test). After a mean follow-up period of 12.5 months (SD: 0.9 months), the surface area of the perforator-based interposition flaps increased to 142%, whereas the surface area of the FTSGs decreased to 92% (95% confidence interval of the difference -76 to -23, $p<0.001$, independent t-test).

Characteristics		Flaps N=16	FTSGs N=14	p-value
Male/Female		8/8	7/7	-
Age patient, mean (SD)		49 (19)	39 (21)	0.183 ¹
Smoker		2	3	0.464 ²
Location	Head/neck	4	5	-
	Arms	5	4	-
	Legs	0	1	-
	Back/Thorax	5	3	-
	Abdomen	2	1	-
Color, mean (SD)		8.9 (4.3)	6.3 (2.9)*	0.071 ¹
Elasticity, mean (SD)		0.7 (0.3)	0.6 (0.4)*	0.775 ³
POSAS observer score, mean (SD)		3.6 (0.8)	4.0 (1.1)	0.254 ¹
POSAS patient score, mean (SD)		5.1 (1.5)	5.9 (1.3)*	0.151 ¹
Range of Motion in degrees (SD)		84 (56)**	92 (75)*	0.976 ³

Table 1. Baseline demographic and clinical characteristics of both treatment groups.
* refers to N=13; preoperative elasticity, color, range of motion measurements and subjective patient score of one patient are lacking. ** refers to N=15; one perforator-based interposition flap was located at the abdomen and did not involve any motion, nor restriction of motion. ¹=Chi-square test ²=Independent t-test, ³= Mann-Whitney U test.

The results of the secondary outcome parameters are shown in Table 2. The width of the flaps was significantly larger than the width of the FTSGs after both 3 and 12 months. Furthermore, the mean POSAS score by the observers was significantly lower (i.e. better in terms of scar quality) for the flaps compared to the FTSGs after both 3 and 12 months. Also, the POSAS score by the patients was better at 3 and 12 months in the flap group, although not statistically significant. The color difference between flaps and normal skin was lower than for FTSGs. No statistically significant differences were found in terms of elasticity, measured with the Cutometer® between the two interventions at both follow-up points.

	Flaps N=16	FTSGs N=12*	95% confidence interval of the difference	p-value
Secondary outcome parameters				
Difference width flap/graft in percentage after 3 months, mean (SD)	124% (19)	95% (11)	-41 to -18	<0.001
Difference width flap/graft in percentage after 12 months, mean (SD)	120% (20)	90% (19)	-76 to -23	0.001
POSAS observer score after 3 months, mean (SD)	1.9 (0.6)	2.4 (0.6)	0.0 to 1.0	0.040
POSAS observer score after 12 months, mean (SD)	1.8 (0.5)	2.8 (1.4)	0.2 to 1.8	0.019
POSAS patient scar score after 3 months, mean (SD)	3.0 (2.1)	3.7 (1.6)	-0.7 to 2.2	0.319
POSAS patient scar score after 12 months, mean (SD)	2.8 (2.0)	3.5 (1.6)	-0.9 to 2.1	0.409
Color after 3 months, mean (SD)	3.7 (3.0)	8.3 (2.8)	2.3 to 6.9	<0.001
Color after 12 months, mean (SD)	2.9 (2.7)	8.1 (4.6)	2.2 to 8.2	0.001
Elasticity after 3 months, mean (SD)	1.2 (0.4)	0.9 (0.7)	-0.8 to 0.1	0.134
Elasticity after 12 months, mean (SD)	0.8 (0.3)	0.8 (0.4)	-0.3 to 0.3	0.969

Table 2. Results of the secondary outcome parameters, measured 3 and 12 months postoperative. The independent t-test was used to calculate the differences. * N=12 because one FTSG was subject to complete necrosis and in one subject secondary outcome measurements are lacking.

Range of motion

In the flap group, the range of motion increased from 84 degrees to 95 degrees ($p=0.012$, Wilcoxon signed ranks test) after 3 months and to 96 degrees ($p=0.041$, Wilcoxon signed ranks test) after 12 months. In the FTSG group the range of motion increased from 92 to 98 degrees ($p=0.074$, Wilcoxon signed ranks test) after 3 months and to 104 degrees ($p=0.114$, Wilcoxon signed ranks test) after 12 months.

Complications

All flaps survived. However, in the FTSG group one graft was subject to complete necrosis. This FTSG required revision surgery. Because the primary outcome as well as the majority of the secondary outcomes could not be measured to any further extent, this patient was subsequently excluded from further analysis. A mean percentage of necrosis of 6% was found for the flap group and 17% for the FTSG group ($p= 0.208$, MWU test). In the patient that suffered from diabetes mellitus, the flap was vascularly compromised 5 days after the operation. The tip became necrotic and the flap was surgically trimmed 9 days after the initial procedure. The initial surface area measurement and consecutive follow-up measurements were performed from that moment on.

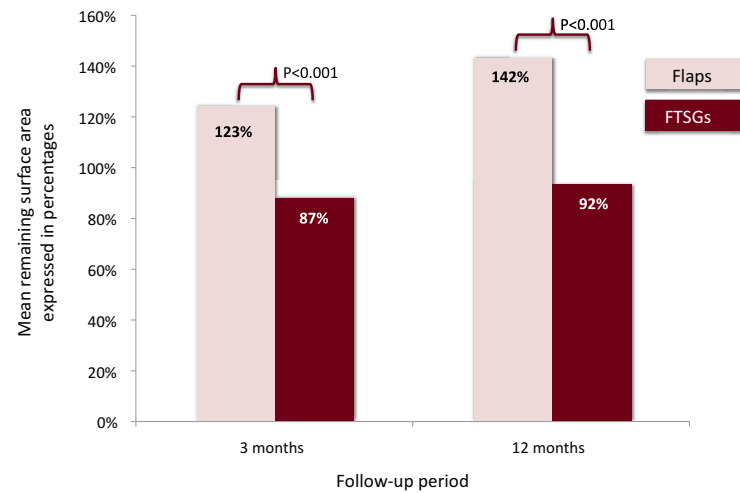


Figure 6. Bar chart representing the change in surface area (%) of the flaps and FTSGs after 3 and 12 months. Accompanying p-values are shown behind the braces.

Discussion

This is the first RCT that investigated the efficacy of perforator-based interposition flaps for the treatment of burn scar contractures. The long-term results showed convincingly that flaps perform better than FTSGs in providing a safe and effective tool to sustainably release burn scar contractures. We observed an increase in surface area of the flaps to 123% after 3 months and a further increase to 142% after 12 months. On the other hand, FTSGs showed a significant contraction; the remaining surface area decreased to 87% after 3 months. After 12 months, the surface area of the FTSGs slightly increased to 92% but was still contracted. The mean surface area differences between the two interventions were statistically significant at 3 and 12 months ($p < 0.001$ at both follow-up moments). The results of this RCT strengthen the conclusions from our pilot study that was previously published¹⁸. In that study, which described the safety and versatility of perforator-based flaps for the reconstruction of scar contractures, an increase in surface area was found¹⁸. Again, we found that the size of the flaps increased with time. This finding merits to be highlighted and shows the sustainability of the technique for scar contracture releasing.

In the present study, the range of motion improved significantly in the flap group after both 3 and 12 months. Additionally, the FTSG group showed improvement in the range of motion, however without being statistically significant. Although both 'range of motion' and 'surface area' are important outcome parameters, we considered surface area to be more appropriate as primary outcome parameter because the range of motion is influenced and

confounded by factors such as stiffness of the joints or contractures in other directions. For this reason, and because range of motion was measured on different locations with diverse ranges (for example neck vs. shoulder), it is in our opinion not appropriate to perform an analysis between the two intervention groups. Nevertheless, the results concerning the range of motion support the results of the primary outcome parameter.

Other studies on the effectiveness of perforator-based interposition flaps for burn scar contracture release demonstrated favorable results. However, in those studies both objective outcome measures and control treatment groups were lacking^{17,19}. The difference in contraction rate between the two interventions can be explained by the following hypothesis: after a release of a burn scar contracture, a considerable defect is generated because of the substantial forces that are exerted in the contracture by the contractile properties of the scar. The created wound bed has the tendency to contract again and the interpositioned tissue (the FTSG or flap) is subject to this contraction process. In contrast to FTSGs, flaps contain subcutaneous fat tissue. It may be hypothesized that the subcutaneous fat acts as a functional sliding layer to prevent the flap from adhering to the underlying wound bed, thereby making it less susceptible to contraction. The presence of subcutaneous fat tissue may also explain the fact that the flaps were found to be more similar to normal skin, as was shown by the secondary outcome parameters.

The treatment algorithm that was used in the present study provides a step-wise approach for the surgical treatment of scar contractures¹⁸. It implies that the base of the interposition flap is left intact, requiring that the flap is not vascularly compromised. The intact skin pedicle supports the blood supply and the venous outflow and, in addition, no unnecessary scar is created. However, when the angle of rotation is too large, the flap should be islanded to prevent an unalterable dog ear and/or a compromised vascularization caused by torsion of the perforator bundle. In this study, conversion to an islanded flap was often not necessary (in only 2 out of 16 interposition flaps), so 14 flaps benefitted from an intact skin base. The option to convert the peninsular flap into an insular flap makes this algorithm extremely versatile. The safety of the perforator-based interposition flaps was particularly underlined by the lower rate of necrosis compared to FTSGs: 6% compared to 17%. Moreover, one FTSG was subject to complete necrosis and needed a re-operation. Although we presume that incorporating the perforator bundle in the interposition flap enhances its safety, we did not prove that the perforator we detected preoperatively, is responsible for the perfusion of the flap. For that purpose we should have dissected the perforator bundle from its surrounding fat tissue. In flaps where the skin base is left intact this is unnecessary and should be discouraged because it may cause unwarranted damage to the perforator bundle.

Since local interposition flaps are more effective, safe and versatile, they should be preferred over FTSGs for the treatment of scar contractures. One limitation of perforator-

based interposition flaps is that sufficient adjacent healthy skin has to be available. However, inclusion of a certain amount of supple scar tissue is possible. In this study, the majority of the flaps (9/16) contained some scar tissue, with a mean surface area of 30%. We did not observe differences in the rate of necrosis and the surface area between flaps that contained scar tissue and flaps that consisted completely of healthy tissue. For the future we anticipate that interposition flaps based on a perforator will become a keystone in reconstructive burn surgery. Because this intervention is relatively easy to perform and has proven to be safe and effective, these flaps may provide a sustainable solution to other challenges such as acute burns in functional areas or large defects that are preferably not closed with a skin graft.

Conclusions

This RCT demonstrated that perforator-based interposition flaps result in a more effective scar contracture release than FTSGs. Therefore, in scar contracture releases where both techniques are interchangeable, we advocate the use of a perforator-based interposition flap over a FTSG.

Acknowledgements

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